REMARKS

1. Claims 1 though 4 have been amended; claims 6-15 are withdrawn. No new matter has been added.

2. The specification is objected to in that certain trademarks are not properly identified as such. Applicants will amend the specification to correct this.

3. Claims 1-5 are rejected under 35 U.S.C §112 as indefinite for failure to particularly recite the "condition mediated by eotaxin." Claim 1 has been amended to specifically identify the condition as being selected from asthma, allergy or allergic disease. Accordingly, Applicants respectfully request that this objection be withdrawn.

4. Claims 1-5 are rejected under 35 U.S.C §112 for lack of enablement. Although the Examiner argues forcefully that the peptides of McDonald, et al., which are not intended or reported to generate an immune response, would neverthless do so inherently (see 5/29/07 Office Action at paragraph 10), the Examiner also argues that generation of antibodies to proteins "remains a challenge". Applicants respectfully submit that the use of vaccines to generate antibodies is a mature art, so that the guidance required is not that great, and that the specification moreover provides a highly detailed teaching in the selection of immunogenic fragments of eotaxin, effective conjugates and methods for making conjugates, effective adjuvants, and optimal formulations.

It is well established that the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). Only after the examiner provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden

shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility. *Id.;* see also *In re Bundy,* 642 F.2d 430, 433, 209 USPQ 48, 51 (CCPA 1981).

In this case, Applicants respectfully submit that the Examiner has not cited any reference or provided any evidence suggesting that the specific methods, which are specifically targeted to this particular address the concerns known in the art, would not work in this case. The evidence cited by the Examiner, a review paper by Francis et al., is not relevant, as this paper relates to the use of peptide antigens to induce *tolerance* in people who have allergies to such proteins; it does not relate to the use of therapeutic vaccines to generate an immune response.

A consideration of the factors set forth in *In re Wands*, 858 F.2d 731 (Fed.Cir. 1988) strongly supports finding of enablement in this case. In *Wands*, the Court of Appeals for the Federal Circuit reversed the Patent Office's finding of nonenablement and identified a variety of factors which may be relevant to whether practicing a claimed invention would require undue experimentation: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. As the *Wands* court held, whether undue experimentation is required is not a single, simple factual determination, and no one factor is necessarily determinative. Rather, enablement or lack of enablement is determined by weighing all of the applicable factual considerations. Applying the *Wands* factors to the instant case, it is clear that practicing the instant invention would not require undue experimentation, as the specificaton provides considerable guidance and exemplification for

making the subject vaccines (albeit no clinical trials), the prior art relating to vaccine production is extensive, the skill of those working in the field is very high, the level of predictability is in some respects greater than for a typical small molecule pharmaceutical in that the claimed method is highly speciic for a target, eotaxin, which is known to be biologically relevant, and the claims address only vaccines for this particular cytokine.

The Examiner argues, however, that "pharmaceutical therapies in the absence of in vivo clinical data are unpredictable" for various reasons, providing a standard that would render most pharmaceutical inventions unpatentable, as such applications are typically filed years before clinical data becomes available. Applicants respectfully submit that the Examiner's suggestion that clinical data is required to demonstrate enablement of pharmaceutical therapies is simply not supported by the Federal Circuit's caselaw.

In a recent case, *Falko-Gunter Falkner v. Inglis,* 448 F.3d 1357 (Fed. Cir 2006)(copy attached), the Federal Circuit addressed the enablement and written description requirements in the context of pharmaceuticals, and vaccines in particular. This case involved an interference directed to a vaccine using a live poxvirus wherein the poxvirus is lacking an essential gene and so cannot replicate except in a helper cell line transformed with the deleted essential poxvirus gene. The junior party in the interference argued that the senior party's disclosure did not satisfy the written description and enablement standards, and thus was not entitled to the earlier filing date. The senior party to the interference did not actually identify any essential poxvirus genes, he had no examples of any poxvirus vaccines, and the specification dealt mostly with herpes viruses, poxvirus vaccines being mentioned only in the general description. The PTO and the Federal Circuit nevertheless found the senior party's application to be enabled. In applying the

Wands factors, the Federal Circuit emphasized that the existence of publications which disclosed poxvirus essential genes was sufficient to provide enablement for the claims of the application, even though such genes were not disclosed specifically in the application. *Id.* at 1365.

As the disclosure in this case is clearly far more specific and detailed than the disclosure for the vaccines claimed in *Falko-Gunter Falkner,* in that the structure of the essential components of the vaccine is defined and set forth clearly, Applicants respectfully submit that the standards for enablement are met in this case, and the rejection for lack of enablement should be withdrawn.

6. Claims 1-5 are rejected under 35 U.S.C §112, first paragraph, as failing to comply with the written description requirement. The Examiner notes that the claims are not limited to vaccines directed to human eotaxin, as disclosed, but to eotaxin of any species. With regard to written description, the Federal Circuit has held that (1) examples are not necessary for written description, (2) actual reduction to practice is not required, and (3) there is no *per se* rule that an invention that involves a biological macromolecule must contain a recitation of known structures. *Falko-Gunter Falkner* , 448 F.3d at 1366. In this case, as the Examiner recognizes, the Applicants have disclosed human eotaxin and a large number of immunogenic human eotaxin fragments. Just as in *Falko-Gunter Falkner* the applicant was permitted to claim poxvirus vaccines, although the disclosure was principally directed to herpes viruses, the failure to disclose all known eotaxin sequences in this case should not give rise to an objection for lack of written description, as the sequences for many species can be readily obtained through a simple search of Genbank or similar public database. To facilitate prosecution, however, the claims have been amended to recite that the species to be treated is a human and the target is

human eotaxin. The essential characteristic linking the disclosed sequences is, of course, that they provide an immunogenic response to the human eotaxin.

Applicants respectfully request that the rejection for lack of written description be withdrawn.

7. Claims 1-5 are rejected under 35 U.S.C. §102(b) for lack of novelty over McDonald, et al. Applicants respectfully note that the compounds of McDonald, although having some structural features in common with the immunogenic conjugates of the present invention, are not and are not intended to be immunogenic conjugates. Rather, they are intended to be cytotoxic drugs, "magic bullets" for killing cells. Eotaxin is identified as a possible ligand, among a host of other cytokines. The compounds of McDonald are generally fusion proteins or otherwise prepared to contain a single moiety of ligand (e.g. eotaxin) linked to a toxin, in contrast to the immunogenic conjugates of the invention herein, which are chemically crosslinked to a large toxin molecule, so that the toxin molecule might contain many moieties of antigen, thereby enhancing its immunogenic potential. The compounds of McDonald are formulated and delivered differently, presumably using biologically neutral pharmaceutical excipients rather than immunogenic adjuvants. Not surprisingly, they have a different biological effect, and would not be suitable for use in the methods claimed in the instant application. Applicants therefore respectfully request that the rejection for lack of novelty over McDonald be withdrawn.

8. Claims 1-5 are rejected under 35 U.S.C. §102(b) for lack of novelty over Bachmann, et al. Applicants note that Bachmann has a filing date of November 7, 2002 and was published on August 21, 2003, although one of the three applications to which it claims priority was filed November 7, 2001. The instant application claims priority to March 25, 2002, and has an

international filing date of March 24, 2003. Accordingly, Bachmann is not properly citable as a reference under 35 U.S.C. §102(b), and Applicants respectfully request that this rejection be withdrawn.

Reconsideration and withdrawal of the pending objections and a speedy allowance of the claims submitted is respectfully requested. The Examiner is invited to contact the undersigned attorney for the Applicants in the event of any questions.

Respectfully submitted,

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